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=> d his

     (FILE 'HOME' ENTERED AT 12:32:25 ON 20 SEP 2004)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:33:13 ON 20 SEP 2004
L1          1263 S AURORA (5W)KINASE?
L2            32 S "AUR-1" OR "AUR-2"
L3          1288 S L1 OR L2
L4           643 S HUMAN AND L3
L5       9998535 S MODULAT? OR INHIBIT? OR ACTIVAT?
L6           298 S L4 AND L5
L7            23 S L6 AND (PATIENT? OR ADMINISTER?)
L8            12 DUP REM L7 (11 DUPLICATES REMOVED)
                 E PLOWMAN G/AU
L9           696 S E3-E10
                 E MOSSIE K/AU
L10           84 S E3-E7
L11          759 S L9 OR L10
L12           18 S L4 AND L11
L13            6 DUP REM L12 (12 DUPLICATES REMOVED)

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NEWS 4	May 12	Polymer links for the POLYLINK command completed in REGISTRY
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NEWS 19	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
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NEWS 21	SEP 14	STN Patent Forum to be held October 13, 2004, in Iselin, NJ

NEWS EXPRESS	JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
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                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

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FILE 'LIFESCI' ENTERED AT 12:33:13 ON 20 SEP 2004
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=> s aurora (5w)kinase?
L1          1263 AURORA (5W) KINASE?

=> s "AUR-1" or "AUR-2"
L2            32 "AUR-1" OR "AUR-2"

=> s l1 or l2
L3          1288 L1 OR L2

=> s human and l3
L4           643 HUMAN AND L3

=> s modulat? or inhibit? or activat?
   3 FILES SEARCHED...
L5       9998535 MODULAT? OR INHIBIT? OR ACTIVAT?

=> s l4 and l5
L6           298 L4 AND L5
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=> s l6 and (patient? or administer?)
L7          23 L6 AND (PATIENT? OR ADMINISTER?)

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8          12 DUP REM L7 (11 DUPLICATES REMOVED)

=> d 1-12 ibib ab

L8   ANSWER 1 OF 12  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:        2004:701991  HCAPLUS
TITLE:                   Tetracyclic pyrazole derivatives as kinase
                         inhibitors, process for their preparation and
                         pharmaceutical compositions comprising them for use
                         in, e.g., cancer therapy
INVENTOR(S):             Vanotti, Ermes; Cervi, Giovanni; Pulici, Maurizio;
                         Menichincheri, Maria; Varasi, Mario; Vianello, Paola
PATENT ASSIGNEE(S):      Pharmacia Italia S.P.A., Italy
SOURCE:                  PCT Int. Appl., 150 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
     ---------------      ----   --------    --------------------   --------
     WO 2004071507         A1    20040826    WO 2004-EP50071        20040203
         W:  AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG,
             BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR,
             CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES,
             ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN,
             IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC,
             LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX,
             MZ, MZ, NA, NI
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
             BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
             MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
             GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN,
             GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                          US 2003-448049P     P  20030217
AB   The invention provides a method for treating diseases caused by and/or
     associated with an altered protein kinase activity which comprises
     administering to a mammal in need thereof an effective amount of a
     tetracyclic pyrazole.  The invention also provides tetracyclic pyrazole
     derivs. of formula I [R1, R2 and R3 independently are H, cyano, carboxy,
     hydroxyaminocarbonyl, (un)substituted amino, carbonyl, sulfonamido, alkyl,
     alkenyl, alkyloxy, carbonyloxy, (hetero)aryl, aryloxy, alkyl/arylthio,
     alkyl/arylsulphinyl, alkyl/arylsulfonyl, (thio)ureido,
     alkyl/arylsulfonylamino, alkyl/arylaminosulfonyl; R1 and R2 also
     independently are halo, nitro, hydroxy; Y is (CH2)n or -CH=CH-; n is 1-3].
     Also disclosed are useful intermediates, a library comprising at least two
     compds. I, a process for their preparation and the pharmaceutical compns.
     containing them, which are useful in the treatment of diseases caused by
     and/or associated with an altered protein kinase activity such as cancer,
     cell proliferative disorders, viral infections, autoimmune diseases and
     neurodegenerative disorders.  Three representative types of I,
     pyrazolocarbazoles, pyrazolocyclopentaindoles and
     pyrazolocycloheptaindoles, have been synthesized, and their
     inhibitions toward cdk2/cyclin A, cdk2/cyclin E, cdk1/cyclin B1,
     cdk5/p25, cdk4/cyclin D1, MAPK, PKA, EGFR, IGF1-R, Aurora-2 and Cdc 7 have
     been carried out to determine the inhibitory activity and specificity
     for the protein kinases (no data).  Thus, treatment of carbazolone II,
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which was prepared from 4-nitroaniline and 2-hydroxymethylenecyclohexanone, with N,N-dimethylformamide di-Et acetal, followed by cyclocondensation with hydrazine, gave pyrazolocarbazole III. Solid-phase synthesis of various pyrazolocarbazoles from III was realized via attaching of III to chlorotrityl resin, reduction of the nitro group to an amino group, coupling with carboxylic acids and finally cleavage from the resin with TFA.

L8 ANSWER 2 OF 12 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2004425809 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15330750
TITLE: Dawn of **Aurora kinase inhibitors** as anticancer drugs.
AUTHOR: Doggrell Sheila A
CORPORATE SOURCE: Doggrell Biomedical Communications, 47 Caronia Crescent, Lynfield, Auckland, New Zealand.. s.doggrell@xtra.co.nz
SOURCE: Expert opinion on investigational drugs, (2004 Sep) 13 (9) 1199-201.
Journal code: 9434197. ISSN: 1744-7658.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20040828
Last Updated on STN: 20040828

AB With the current standard chemotherapy regimens only approximately 25% of acute myelogenous leukaemia (AML) **patients** survive > 5 years. **Aurora kinases** are overexpressed in many **human** cancers. VX-680 **inhibited** Aurora-A, -B, -C and the FMS-like tyrosine kinase-3 with apparent **inhibitory** constants of 0.6, 18, 4.6 and 30 nM, respectively. In primary leukaemia cells from **patients** with AML, which were refractory to standard therapies, VX-680 **inhibited** colony formation. In nude mice, VX-680 markedly reduced **human** AML tumours. The development of VX-680 for use in AML should continue.

L8 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:377008 HCAPLUS
DOCUMENT NUMBER: 138:380373
TITLE: Gene expression profiling in **human** lung cancer, and therapeutic and diagnostic uses
INVENTOR(S): Beebe, Jean S.; Coleman, Kevin G.; Dmitrovsky, Ethan; Turi, Thomas G.
PATENT ASSIGNEE(S): Pfizer Products Inc., USA; Trustees of Dartmouth College
SOURCE: PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040317	A2	20030515	WO 2002-US35149	20021102

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,

NE, SN, TD, TG

US 2003219768	A1	20031127	US 2002-286989		20021102
PRIORITY APPLN. INFO.:			US 2001-335317P	P	20011102
			US 2001-336024P	P	20011102
			US 2001-336298P	P	20011102

AB The present invention provides genes that are differentially expressed during lung neoplasia. These genes and gene products comprise panels for use in screening candidate agents for therapeutic intervention in lung cancers, and for use in therapeutic, prognostic and diagnostic methods and compns. The present invention specifically relates to TRK-B (GenBank number U12140) and to Aur2 (RefSeq number NM_003600, GenBank nos. AF011468, AF008551, BC001280) and/or their encoded gene product, which were identified by gene expression profiling as being differentially expressed during neoplasia of lung cells. Therapeutic agents are also provided by the invention. Diagnostic compns. include compns. comprising detection agents for detecting one or more genes that have been shown to be up- or down-regulated in pathogenesis of lung cancer. Exemplary detection agents include nucleic acid probes, which can be in solution or attached to a solid surface, e.g., in the form of a microarray. The invention also provides computer-readable media comprising values of levels of expression of one more genes that are **modulated** in lung cancer.

L8 ANSWER 4 OF 12 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER:	2003166610 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 12684414
TITLE:	**Activation** and overexpression of centrosome kinase BTAK/Aurora-A in **human** ovarian cancer.
AUTHOR:	Gritsko Tatiana M; Coppola Domenico; Paciga June E; Yang Lin; Sun Mei; Shelley Sue A; Fiorica James V; Nicosia Santo V; Cheng Jin Q
CORPORATE SOURCE:	Department of Pathology and Molecular Oncology Program, H Lee Moffitt Cancer Center and Research Institute, College of Medicine, University of South Florida, Tampa, Florida 33612, USA.
CONTRACT NUMBER:	CA77935 (NCI) CA89242 (NCI)
SOURCE:	Clinical cancer research : an official journal of the American Association for Cancer Research, (2003 Apr) 9 (4) 1420-6. Journal code: 9502500. ISSN: 1078-0432.
PUB. COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	200401
ENTRY DATE:	Entered STN: 20030410 Last Updated on STN: 20040121 Entered Medline: 20040120

AB Previous studies have demonstrated amplification of the centrosome serine/threonine kinase BTAK/Aurora-A in 10-25% of ovarian cancers. However, alterations of BTAK/**Aurora**-A at **kinase** and protein levels and its role in ovarian cancer progression have not been well documented. In this study, we examined the kinase activity and protein levels of BTAK/Aurora-A in 92 **patients** with primary ovarian tumors. In vitro kinase analyses revealed elevated BTAK/**Aurora**-A **kinase** activity in 44 cases (48%). Increased BTAK/Aurora-A protein levels were detected in 52 (57%) specimens. High protein levels of BTAK/**Aurora**-A correlated well with elevated **kinase** activity. **Activation** and overexpression of BTAK/Aurora-A were more frequently detected in early stage/low-grade ovarian tumors, although there was no statistic significance at the kinase level between early stage/low-grade and late stage/high-grade tumors. Moreover, BTAK/Aurora-A was preferentially expressed in noninvasive tumors, as revealed by immunohistochemical staining, suggesting that

alterations of BTAK/Aurora-A could be an early event in **human** ovarian oncogenesis. To our knowledge, this is the first demonstration of recurrent **activation** and overexpression of BTAK/Aurora-A in **human** ovarian cancer, which may play a critical role in development of this malignancy.

L8 ANSWER 5 OF 12 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2003126665 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12631597
TITLE: Overexpression of oncogenic STK15/BTAK/**Aurora** A **kinase** in **human** pancreatic cancer.
AUTHOR: Li Donghui; Zhu Jijiang; Firozi Pervez F; Abbruzzese James L; Evans Douglas B; Cleary Karen; Friess Helmut; Sen Subrata
CORPORATE SOURCE: Department of Gastrointestinal Medical Oncology, The University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030, USA.. dli@mdanderson.org
CONTRACT NUMBER: CA 89716 (NCI)
R01 CA 61979 (NCI)
SOURCE: Clinical cancer research : an official journal of the American Association for Cancer Research, (2003 Mar) 9 (3) 991-7.
Journal code: 9502500. ISSN: 1078-0432.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 20030319
Last Updated on STN: 20031004
Entered Medline: 20031003

AB PURPOSE: Multiple chromosome abnormalities, including gain of chromosome20q, have been detected frequently in **human** pancreatic cancers. Overexpression of the STK15/BTAK/Aurora A gene located on chromosome 20q13, which encodes a centrosome-associated serine/threonine kinase, has been shown to induce chromosomal instability, leading to aneuploidy and cell transformation in multiple in vitro experimental systems. The purpose of this study was to investigate the expression and copy number alteration of STK15 in pancreatic cancer. EXPERIMENTAL DESIGN: STK15 expression at both the mRNA and protein levels together with the copy number of STK15 gene was measured in nine pancreatic carcinoma cell lines: (a) HPAF-II; (b) Aspc-1; (c) Panc-1; (d) Panc-3; (e) Panc-28; (f) Panc-48; (g) HS766T; (h) MIAPaCa-2; and (i) BxPc3. STK15 protein expression was also examined in normal pancreatic tissues and tumors by Western blotting and immunohistochemistry. RESULTS: STK15 was overexpressed in all of the nine cell lines examined, but gene amplification was infrequent. Western Blot analysis of primary tumor tissues revealed 2-10 times overexpression of STK15 protein compared with normal adjacent tissues from pancreatic cancer **patients**. Concurrent overexpression of cdc20, an STK15-associated protein, and reduced expression of cdc25, a mitosis-**activating** protein phosphatase, were detected in the same tumor samples. Elevated STK15 protein expression was detected in 22 of 38 tumor sections (58%) from pancreatic cancer **patients**. The extent of STK15 expression was not significantly correlated with the size, degree of differentiation, and metastasis status of the tumors. CONCLUSIONS: These results show that STK15 is overexpressed in pancreatic tumors and carcinoma cell lines and suggest that overexpression of STK15 may play a role in pancreatic carcinogenesis.

L8 ANSWER 6 OF 12 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:151959 BIOSIS

DOCUMENT NUMBER: PREV200400147614
TITLE: VX-680, a novel kinase **inhibitor**, induces remission in an oncogene-driven (Flt3-ITD) murine leukemia model.
AUTHOR(S): Furey, Brinley F. [Reprint Author]; Ma, Jianguo [Reprint Author]; Firestone, Brant G. [Reprint Author]; Henkel, Greg [Reprint Author]; Ramachandran, Ravi [Reprint Author]; Shames, Benjamin [Reprint Author]; Boucher, Diane [Reprint Author]; Yao, Yao [Reprint Author]; Harding, Matthew [Reprint Author]; Yao, Megan [Reprint Author]
CORPORATE SOURCE: Vertex Pharmaceuticals Inc, Cambridge, MA, USA
SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 621a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004

AB INTRODUCTION: Several mutations have been associated with increased **activation** of **aurora kinases** in **human** malignancies, rendering this kinase family an attractive target for anti-cancer therapies. The **Aurora kinases** are three highly homologous serine/threonine kinases that play a critical role in cell division. Aurora A and B are essential for mitotic spindle formation and chromosome alignment, while the function of Aurora C remains unclear. VX-680 is a small molecule reversible **inhibitor** that targets aurora A, B, and C with Ki values of 0.7, 18, and 4.6 nM, respectively. VX-680 also **inhibits** activity of Flt3 (Ki=30 nM), a receptor tyrosine kinase essential for hematopoietic growth and differentiation. An **activating** mutation in the Flt3 gene is found in 30% of all acute myeloid leukemia (AML) **patients**. In vitro, VX-680 demonstrates potent **inhibitory** activity (IC50=12.4 nM) against MV411 leukemia cells, a **human** tumor cell line derived from primary AML **patient** blast samples. The present in vivo study was conducted to test VX-680 in a murine leukemia model using BaF3 cells transduced with an **activating human** Flt-3 mutation. METHODS: BaF3/Flt3-ITD cells (1X106) were injected i.v. into male Balb/c mice on Day 0. All treatments began 5.5 days following cell implantation. VX-680 treatment was initiated at 45 and 15 mg/kg (i.p., BID) in 3-day cycles, biweekly. In an additional group, VX-680 was **administered** at 75 mg/kg (i.p., BID) every other day after an initial 2-day dosing period. Doxorubicin (3 mg/kg, weekly), a standard AML therapy, and MLN518 (60 mg/kg BID), a selective Flt3 **inhibitor**, were tested as reference compounds. All treatments were discontinued on day 42 following implantation. A subset of animals from the 75 and 45 mg/kg groups were kept for daily monitoring, while the remaining animals were sacrificed. Using probes for the **human** Flt3-ITD, RQT-PCR was performed on spleen lysates from sacrificed animals. RESULTS: Survival time of vehicle controls ranged from 21 to 25 days, with a median survival of 21 days. Doxorubicin, MLN518, and 15 mg/kg VX-680 significantly increased median survival to 38, 34.5, and 31 days, respectively. Notably, all animals treated with 45 or 75 mg/kg VX-680 were alive on Day 42 when treatment was discontinued. Quantitative PCR analysis on spleen lysates from sacrificed animals revealed no minimum residual disease in the 75 mg/kg group (0/4). In the 45 mg/kg group, two out of five animals (2/5) had undetectable levels of the Flt-3 ITD. Importantly, 38 days after treatment was discontinued (day 80), remission rates for the 75 mg/kg and 45 mg/kg groups were 100% (5/5) and 33% (2/6), respectively. CONCLUSION: VX-680 provided a significant increase in survival in all dose groups. In

addition, when treated with 75 mg/kg every other day, animals experienced 100% survival and sustained remission for 38 days following treatment discontinuation. As an **inhibitor** of both **aurora** and Flt3 **kinases**, VX-680 may be a promising new therapeutic option for the treatment of hematological malignancies. Additional studies are currently underway to determine the optimal dosing regimen and to further evaluate the biochemical effects of VX-680 on downstream substrates of **aurora** and Flt-3 **kinases**.

L8 ANSWER 7 OF 12 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2003:205217 BIOSIS
DOCUMENT NUMBER: PREV200300205217
TITLE: Targeting aurora2 kinase in oncogenesis: A structural bioinformatics approach to target validation and rational drug design.
AUTHOR(S): Vankayalapati, Hariprasad; Bearss, David J.; Saldanha, Jose W.; Munoz, Ruben M.; Rojanala, Sangeeta; Von Hoff, Daniel D.; Mahadevan, Daruka [Reprint Author]
CORPORATE SOURCE: Arizona Cancer Center, University of Arizona, 1515 North Campbell Avenue, Tucson, AZ, 85724, USA
dmahadevan@azcc.arizona.edu
SOURCE: Molecular Cancer Therapeutics, (March 2003) Vol. 2, No. 3, pp. 283-294. print.
ISSN: 1535-7163 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Apr 2003
Last Updated on STN: 10 Jun 2003

AB The **aurora kinases** are a novel oncogenic family of mitotic serine/threonine kinases (S/T kinases) that are overexpressed in a number of solid tumors, including pancreas and colorectal cancer. A PSI-BLAST search (National Center for Biotechnology Information (NCBI)) with the sequence of the S/T kinase domain of **human** auroral kinase (also known as AUR1, ARK2, AIk2, AIM-1, and STK12) and **human** aurora2 kinase (also known as AUR2, ARK1, AIK, BTAK, and STK15) showed a high sequence similarity to the three-dimensional structures of bovine cAMP-dependent kinase (Brookhaven Protein Data Bank code 1CDK), murine cAMP-dependent kinase (1APM), and Caenorhabditis elegans twitchin kinase (1KOA). When the auroral or aurora2 sequence was input into the tertiary structure prediction programs THREADER and 3D-PSSM (three-dimensional position-sensitive scoring matrix), the top structural matches were 1CDK, 1APM, and 1KOA, confirming that these domains are structurally conserved. The structural models of auroral and aurora2 were built using 1CDK as the template structure. Molecular dynamics and docking simulations, targeting the ATP binding site of aurora2 with adenylyl imidodiphosphate (AMP-PNP), staurosporine, and six small molecular S/T kinase **inhibitors**, identified active-site residues that interact with these **inhibitors** differentially. The docked structures of the aurora2-AMP-PNP and aurora2-staurosporine complexes indicated that the adenine ring of AMP-PNP and the indolocarbazole moiety of staurosporine have similar positions and orientations and provided the basis for the docking of the other S/T kinase **inhibitors**. **Inhibitors** with isoquinoline and quinazoline moieties were recognized by aurora2 in which H-89 and 6,7-dimethoxyquinazoline compounds exhibited high binding energies compared with that of staurosporine. The calculated binding energies for the docked small-molecule **inhibitors** were qualitatively consistent with the IC50 values generated using an in vitro kinase assay. The aurora2 structural model provides a rational basis for site-directed mutagenesis of the active site; design of novel H-89, staurosporine, and quinazoline analogues; and the screening of the available chemical database for the identification of other novel, small-molecular entities.

L8 ANSWER 8 OF 12 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2003-01840 BIOTECHDS
TITLE: Novel isolated polypeptide, designated NOVX, useful for treating or preventing in NOVX-associated disorders e.g. cardiomyopathy, atherosclerosis, diabetes, cancer, allergy, asthma, Crohn's disease;
vector-mediated recombinant protein-NOVX gene transfer and expression in host cell for disease diagnosis, prognosis, gene therapy and functional proteomics
AUTHOR: EDINGER S; MACDOUGALL J R; MILLET I; ELLERMAN K; STONE D J; GERLACH V; GROSSE W M; ALSOBROOK J P; LEPLEY D M; RIEGER D; BURGESS C E; CASMAN S J; SPYTEK K A; BOLDOG F L; LI L; PADIGARU M; MISHRA V; PATTURAJAN M; SHENOY S; RASTELLI L; TCHERNEV V T; VERNET C A M; ZERHUSEN B D; MALYANKAR U M; GUO X; MILLER C E; GANGOLLI E A
PATENT ASSIGNEE: CURAGEN CORP
PATENT INFO: WO 2002057450 25 Jul 2002
APPLICATION INFO: WO 2001-US48922 29 Nov 2001
PRIORITY INFO: US 2001-327456 28 Nov 2001; US 2000-253834 29 Nov 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-590741 [63]
AB DERWENT ABSTRACT:
NOVELTY - An isolated polypeptide (I), termed NOVX (NOV1-12) comprising a 933, 933, 2281, 855, 2300, 1446, 403, 442, 272, 331, 355, 668, 963, 238, 238 or 1907 residue amino acid sequence (S3), given in the specification, a variant of S1, a mature form of S1 (its variant), is new.

DETAILED DESCRIPTION - An isolated polypeptide (I), termed NOVX (NOV1-12) comprising a 933, 933, 2281, 855, 2300, 1446, 403, 442, 272, 331, 355, 668, 963, 238, 238 or 1907 residue amino acid sequence (S3), given in the specification, a variant of S1, a mature form of S1 (its variant), is new. (I) comprises S1, a variant of S1, a mature form of S1, or a variant of the mature form of S1, where one or more amino acids in the variant of S1 or the variant of the mature form of S1, differs from S1 or the mature form of S1 by not more than 15 % of the amino acid residues. INDEPENDENT CLAIMS are also included for the following: (1) an isolated nucleic acid molecule (II) comprising a nucleic acid sequence encoding (I), comprising a nucleic acid fragment encoding at least a portion of (I) or its variant, or a nucleic acid molecule comprising the complement; (2) a vector (III) comprising (II); (3) a cell (IV) comprising (III); (4) an antibody (V) that binds immunospecifically to (I); (5) determining (M1) the presence or amount of (II) in a sample; (6) identifying an agent that **modulates** the expression or activity of (I); (7) **modulating** an activity of (I), by contacting a cell sample expressing (I) with a compound that binds to (I); (8) a pharmaceutical composition (VI) comprising (I), (II) or (V); (9) a kit comprising (VI) in one or more containers; and (10) treating a pathological state in a mammal, by **administering** to the mammal a polypeptide having an amino acid sequence at least 95 % identical to a polypeptide comprising S1, or its biologically active fragment.

WIDER DISCLOSURE - (1) an oligonucleotide which includes at least 6 contiguous nucleotides of (II); (2) a method to identify specific cell or tissue types based on the expression of NOVX; (3) a nucleic acid molecule that differs from S2 due to degeneracy of the genetic code; (4) a nucleic acid molecule encoding NOVX that contain changes in amino acid residues that are not essential for activity; (5) an isolated antisense nucleic acid molecule hybridizable or complementary to S2, or its fragment, analog or derivatives; (6) biologically active portions, derivatives, fragments, analogs, or homologs of (I); (7) NOVX chimeric or fusion proteins; (8) fragments of (V); (9) an immunoconjugate comprising (V) conjugated to a cytotoxic agent; and (10) novel agents identified by screening assays.

BIOTECHNOLOGY - Preparation: (I) is prepared by standard recombinant techniques. Preferred Polypeptide: NOV1 is homologous to transmembrane

receptor UNC5H2-like family of proteins, NOV2 is homologous to protein tyrosine phosphatase precursor-like family of proteins, NOV3 is homologous to **human** homolog of the Drosophila pecanex family of proteins, and NOV4 is homologous to **Aurora**-related **kinase** 1-like proteins. NOV5 is homologous to 26S protease regulatory subunit 4-like family of proteins, NOV6 is homologous to MITSUGUMIN29-like family of proteins, NOV7 is homologous to Wnt-15-like family of proteins, and NOV8 is homologous to membranes of the Wnt-14-like family of proteins. NOV9 is homologous to beta-adrenergic receptor kinase-like family of proteins, NOV10 is homologous to alpha-mannosidase-like family of proteins, NOV11 is homologous to C1q-related factor-like family of proteins, and NOV12 is homologous to plexin-1 like family of proteins. (I) comprises the amino acid sequence of a naturally occurring allelic variant of S1, where the allelic variant comprises a sequence that is the translation of a nucleic acid sequence differing by a single nucleotide from a 2860, 2860, 6994, 2565, 6903, 4538, 1500, 1500, 1020, 1020, 1085, 2037, 3003, 805, 805 or 5895 base pair sequence (S2), given in the specification. The sequence of the variant comprises a conservative amino acid substitution. Preferred Polynucleotide: (II) comprises the sequence of a naturally-occurring allelic variant, and encodes a polypeptide comprising the sequence of a naturally-occurring polypeptide variant. (II) differs by a single nucleotide from S2. (II) is selected from S2, a sequence differing by one or more nucleotides from S2, provided that not more than 20 % of the nucleotides differ from S2, and fragments of the sequences. (II) hybridizes under stringent conditions to S2 or its complement. (II) comprises a sequence selected from a first nucleotide sequence comprising a coding sequence differing by one or more sequences encoding S1, provided that not more than 20 % of the nucleotides in the coding sequence in the first nucleotide sequence differ from the coding sequence, an isolated second polynucleotide that is a complement of the first polynucleotide, and a fragment of the sequences. Preferred Vector: (III) further comprises a promoter operably-linked to (II). Preferred Antibody: (V) is preferably monoclonal or humanized antibody. Preferred Method: In (M1), presence or amount of nucleic acid molecule is used as a marker for cell or tissue type which is cancerous.

ACTIVITY - Neuroprotective; Nootropic; Antiparkinsonian; Hypotensive; Hypertensive; Hemostatic; Cardiant; Antianginal; Dermatological; Immunosuppressive; Antiinflammatory; Virucide; Antibacterial; Antiparasitic; Antiallergic; Antiasthmatic; Antirheumatic; Antiarthritic; Anti-HIV (**human** immunodeficiency virus); Vulnerary; Anorectic; Antidiabetic; Immunomodulator; Antipsoriatic; Nephrotropic; Kerolytic; Antiulcer; Cerebroprotective; Anticonvulsant; Antiinfertility; Antimanic; Antidepressant; Metabolic; Cytostatic; Tranquilizer; Analgesic.

MECHANISM OF ACTION - Gene therapy; Vaccine. No biological data is given.

USE - (I) is useful for identifying an agent that binds to (I), by contacting (I) with the agent, and determining if the agent binds to (I), where the agent is a cellular receptor or downstream effector. (I) and (II) are useful for determining the presence or predisposition to a disease associated with altered levels of (I) or (II), especially cancer, in a first mammalian subject. The method comprises measuring the level of expression of (I) or amount of (II) in a sample from the first mammalian subject, and comparing it to the amount of polypeptide or nucleic acid present in a control sample from a second mammalian subject known not to have, or not to be predisposed to, the disease, where an alteration in the expression level of (I) or (II) in the first subject when compared to the control sample indicates the presence of or predisposition to the disease. (I), (II) and (V) are useful for treating or preventing NOVX-associated disorder in the subject preferably **human**, where the disorder is cardiomyopathy, atherosclerosis, diabetes or a disorder related to cell signal processing and metabolic pathway **modulation**. (V) is useful for determining the presence or amount

of (I) in a sample by determining the presence or amount of (V) bound to (I), and for treating a pathological state in a mammal. (All claimed). (I), (II) and (V) are useful for treating or preventing Alzheimer's disease, Parkinson's disorder, hypertension, hypotension, idiopathic thrombocytopenic purpura, hemophilia, heart failure, angina pectoris, myocardial infarction, scleroderma, aortic stenosis, subaortic stenosis, transplantation, autoimmune disease, lupus erythematosus, viral, bacterial, parasitic infections, autoimmune disease, allergies, graft versus host disease, asthma, adult respiratory distress syndrome (ARDS), inflammation, rheumatoid arthritis, multiple sclerosis, acquired immunodeficiency syndrome (AIDS), wound repair, obesity, diabetes, endocrine disorders, anorexia, bulimia, glomerulonephritis, polycystic kidney disease, hypercalceimia, Lesch-Nyhan syndrome, trauma, Crohn's disease, cachexia, psoriasis, actinic keratosis, urinary retention, ulcers, stroke, Huntington's disease, epilepsy, addition, anxiety, pain, stroke, fertility, schizophrenia, manic depression, dementia, Gilles de la Tourette syndrome and cancers. (I) and (II) are useful for screening for molecules, which **inhibit** or enhance NOVX activity or function, and as targets for the identification of small molecules that **modulate** or **inhibit**, e.g. neurogenesis, cell differentiation, cell proliferation, hematopoiesis, wound healing or angiogenesis. (II) is useful in screening assays, detection assays (e.g. chromosomal mapping, tissue typing, forensic biology), predictive medicine (e.g. diagnostic assays, prognostic assays, monitoring clinical trials and pharmacogenomic), and in methods of treatment (e.g. therapeutic and prophylactic). (I) is useful as immunogen to produce antibodies immunospecific for (I), to screen for potential agonist and antagonist compounds, and as bait protein in a two-hybrid or three-hybrid assay. (II) is useful in gene therapy, to express (I), to detect NOVX mRNA or a genetic lesion in NOVX gene, and to **modulate** NOVX activity. (IV) is useful for producing non-**human** transgenic animals which are useful for studying the function and/or activity of NOVX protein and for identifying and/or evaluating **modulators** of NOVX protein activity. (V) is useful for isolating, and purifying (I) and to monitor protein levels in tissue as part of a clinical testing procedure, e.g. for determining the efficacy of treatment regimen.

ADMINISTRATION - (I), (II) or (V) is **administered** by parenteral e.g., intravenous, intradermal, subcutaneous, oral (e.g., inhalation), transdermal, transmucosal or rectal route. No dosage details are given.

EXAMPLE - Identifying isolated nucleic acids, designated NOVX was as follows. The novel NOVX target sequences were subjected to the exon linking process to confirm the sequence. Polymerase chain reaction (PCR) primers were designed by starting at the most upstream sequence available, for the forward primer, and at the most downstream sequence available for the reverse primer. In each case, the sequence was examined, walking inward from the respective termini toward the coding sequence, until a suitable sequence that was either unique or highly selective was encountered, or in the case of the reverse primer, until the stop codon was reached. Such primers were designed based on in silico predictions for the full length cDNA, part (one or more exons) of the DNA or protein sequence of the target sequence, or by translated homology of the predicted exons to closely related **human** sequences form other species. These primers were then employed in PCR amplification. The resulting amplicons were gel purified, cloned and sequenced to high redundancy. The PCR product derived from exon linking was cloned into the pCR2.1 vector. The resulting bacterial clone had an insert covering the entire open reading frame cloned into the pCR2.1 vector. The resulting sequences from all clones were assembled with themselves, with other fragments in CuraGen Corporation's database and with public expression sequence tags (ESTs). Fragments and ESTs were included as components for an assembly when the extent of their identity with another component of the assembly was at least 95 % over 50 base pairs. In addition, sequence traces were evaluated manually and edited for corrections if appropriate.

A sequence comprising 2860, 2860, 6994, 2565, 6903, 4538, 1500, 1500, 1020, 1020, 1085, 2037, 3003, 805, 805 or 5895 base pairs, given in the specification was obtained. (353 pages)

L8 ANSWER 9 OF 12 MEDLINE on STN
ACCESSION NUMBER: 2002464930 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12208897
TITLE: Amplification/overexpression of a mitotic kinase gene in **human** bladder cancer.
AUTHOR: Sen Subrata; Zhou Hongyi; Zhang Ruo-Dan; Yoon Dong S; Vakar-Lopez Funda; Ito Shigemi; Jiang Feng; Johnston Dennis; Grossman H Barton; Ruifrok Arnout C; Katz Ruth L; Brinkley William; Czerniak Bogdan
CORPORATE SOURCE: Division of Pathology and Laboratory Medicine, The University of Texas M. D. Anderson Cancer Center, Houston 77030, USA.
CONTRACT NUMBER: R01CA41424 (NCI)
R01CA61979 (NCI)
R01CA66723 (NCI)
R01CA89716 (NCI)
U01CA85078 (NCI)
SOURCE: Journal of the National Cancer Institute, (2002 Sep 4) 94 (17) 1320-9.
Journal code: 7503089. ISSN: 0027-8874.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020913
Last Updated on STN: 20021001
Entered Medline: 20020930

AB BACKGROUND: The mitotic kinase-encoding gene STK15/BTAK/ AuroraA is associated with aneuploidy and transformation when overexpressed in mammalian cells. STK15 overexpression **activates** an unknown oncogenic pathway that involves centrosome amplification and results in missegregation of chromosomes. Because clinical prognosis and tumor aneuploidy are tightly linked in **human** bladder cancer, we examined whether increased STK15 copy number and protein levels are linked to aneuploidy in bladder cancers. METHODS: STK15 protein was visualized by immunohistochemistry in 205 formalin-fixed, paraffin-embedded **human** bladder tumors. STK15 gene copy number was evaluated in 61 tumors by Southern blot hybridization and in 21 of these 61 tumors by fluorescence in situ hybridization (FISH). Copy numbers of chromosomes 3, 17, 20, and 21 were evaluated by FISH with chromosome-specific probes. STK15 expression levels were related to histologic grade, stage, and DNA ploidy of the tumors and to the **patients**' follow-up data. The chi-square test for association was used to analyze the relationship between STK15 expression and pathologic features. All statistical tests were two-sided. RESULTS: Tumors with low levels of STK15 amplification (3-4 copies) showed minimal deviation in their chromosome copy number and diploid or near-diploid total nuclear DNA content. Tumors with higher levels of STK15 amplification (>4 copies) had a major increase of chromosome copy number and of their total nuclear DNA content, i.e., exhibited pronounced aneuploidy. Elevated expression of STK15 was strongly associated with parameters of clinical aggressiveness including high histologic grade (P<.001), invasion (P<.001), increased rate of metastasis (P<.001), and decreased metastasis-free (P<.001) and overall (P<.001) survival of **patients** with bladder cancer. CONCLUSION: STK15 gene amplification and associated increased expression of the mitotic kinase it encodes are associated with aneuploidy and aggressive clinical behavior in **human** bladder cancer.

L8 ANSWER 10 OF 12 MEDLINE on STN

ACCESSION NUMBER: 2002678101 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12438709
TITLE: Search for the second Peutz-Jeghers syndrome locus: exclusion of the STK13, PRKCG, KLK10, and PSCD2 genes on chromosome 19 and the STK11IP gene on chromosome 2.
AUTHOR: Buchet-Poyau K; Mehenni H; Radhakrishna U; Antonarakis S E
CORPORATE SOURCE: Division of Medical Genetics, Geneva University Medical School, and University Hospitals, Geneva, Switzerland.
SOURCE: Cytogenetic and genome research, (2002) 97 (3-4) 171-8. Journal code: 101142708. ISSN: 1424-8581.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20021120
Last Updated on STN: 20030110
Entered Medline: 20030109

AB Pathogenic mutations in the serine/threonine kinase STK11 (alias LKB1) cause Peutz-Jeghers syndrome (PJS) in most affected individuals. However, in a considerable number of PJS-**patients** mutations cannot be detected in STK11 suggesting genetic heterogeneity. One PJS family without STK11 mutations (PJS07) has previously been described with significant evidence for linkage to a second potential PJS locus on 19q13.3-->q13.4. In this study we investigated candidate genes within markers D19S180 and D19S254, since multipoint linkage analysis yielded significant LOD scores for this region in this family. Four genes in the region (cytohesin 2: PSCD2, kallikrein 10: KLK10, protein kinase C gamma: PRKCG, and serine/threonine kinase 13: STK13) potentially involved in growth **inhibitory** pathways or in the pathophysiology of cancer, were considered as candidates. We first determined the genomic structure of the PSCD2 and PRKCG genes, and performed mutation analysis of all exons and exon-intron junctions of the four genes, in the PJS07 family. No pathogenic mutation was identified in these four genes in affected individuals. A very rare polymorphism resulting in a conserved amino acid change Lys to Arg was found in PSCD2. These data provide considerable evidence for exclusion of these four genes as candidates for the second locus on 19q13.3-->q13.4 in PJS. Finally, we also excluded the recently identified STK11-interacting protein gene (STK11IP, alias LIP1) mapped in 2q36 as candidate for PJS in the PJS07 family, although this could be a good candidate in other non-STK11/LKB1 families.

L8 ANSWER 11 OF 12 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2003:335948 BIOSIS
DOCUMENT NUMBER: PREV200300335948
TITLE: The Association of Survivin's Expression with **Aurora Kinase** 2 and Their Involvement in Cell Survival in Aggressive Non-Hodgkin's Lymphoma.
AUTHOR(S): Hamada, Makoto [Reprint Author]; Yakushijin, Yoshihiro [Reprint Author]; Ohtsuka, Masaki [Reprint Author]; Yasukawa, Masaki [Reprint Author]; Fujita, Shigeru [Reprint Author]; Sakai, Akira [Reprint Author]; Ishimaru, Fumihiko [Reprint Author]
CORPORATE SOURCE: First Department of Internal Medicine, Ehime University School of Medicine, Onsen-gun, Ehime, Japan
SOURCE: Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 1348. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Jul 2003
Last Updated on STN: 23 Jul 2003

AB The **Inhibitor** of Apoptosis Proteins (IAPs) have been proposed to be involved not only in cell survival but also in cell cycle regulation with other centromere proteins, such as **Aurora kinases** . Recently, over-expression of **Aurora Kinases** has been reported in several solid tumors, indicating that the investigation of IAPs and **Aurora Kinases** and their relation might be of potential interest in tumorgenesis. In the present study, we studied mRNA expression of Survivin as an IAP, other anti-apoptosis proteins (Bcl-2, Bcl-6) and **Aurora Kinases** in non-Hodgkin's lymphoma (NHL) compared to normal lymphocytes using Northern blot and Real-time PCR techniques. A total of fifty-seven NHL samples (indolent=21, aggressive low or low-intermediate=13, aggressive high-intermediate or high=19, highly aggressive=4) of single tumor cell suspension from the **patients** with B-cell NHL and nine benign controls were examined. Only Survivin and **Aurora Kinase** 2 mRNA were significantly over-expressed in clinically aggressive types of NHL, and both expressions were strongly correlated with each other (Speamann:0.81, P<.0001). Moreover, in vitro analysis indicated that under-regulation of **Aurora Kinase** 2 mRNA either with an antisense oligonucleotide or with antisense stable transfection induced under-regulation of Survivin and G0/G1 cell cycle accumulation (G0/G1 rate in stable transfection: 74.5% vs. in vector-only stable transfection: 32.5%) in a NHL cell line. Antisense oligonucleotide treatment of Survivin also induced under-regulation of **Aurora Kinase** 2 mRNA and G0/G1 cell cycle accumulation. These results suggest that the expression of Survivin and **Aurora Kinase** 2 is strongly associated with the cell cycle regulation and the **patient** prognosis in aggressive types of NHL.

L8 ANSWER 12 OF 12 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2000251311 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10788588
TITLE: Cell cycle molecular targets in novel anticancer drug discovery.
AUTHOR: Buolamwini J K
CORPORATE SOURCE: Department of Medicinal Chemistry, and Research Institute of Pharmaceutical Sciences, School of Pharmacy, University of Mississippi, Mississippi, MS 38677, USA.
CONTRACT NUMBER: CA80730 (NCI)
SOURCE: Current pharmaceutical design, (2000 Mar) 6 (4) 379-92.
Ref: 79
Journal code: 9602487. ISSN: 1381-6128.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000616
Last Updated on STN: 20000616
Entered Medline: 20000602

AB A number of potential molecular targets for novel anticancer drug discovery have been identified in cell cycle control mechanisms. Prominent among these are the regulatory proteins, cyclins and their effector counterparts the cyclin dependent kinases (CDKs). Aberrant expression of these proteins, particularly cyclins involved in the G1 phase of the cell cycle, namely the D and E cyclins, has been associated with a variety of **human** cancers, including breast and colorectal

cancer, B-lymphoma, prostate and non-small cell lung cancer. **Inhibition** of CDK kinase activity has turned out to be the most productive strategy for the discovery and design novel anticancer agents specifically targeting the cell cycle. Other potentially useful cell cycle areas for exploration include cyclin-CDK interactions, Cdc25 **activation** of cyclin-CDK complexes, ubiquitin-mediated proteolysis of cyclins, cell cycle check point kinases like Chk1, and recently identified oncogenic cell cycle-related **aurora** and polo-like **kinases**. Potent specific **inhibitors** have been identified that bind to the ATP site of CDKs, mainly cyclin B-CDK1, cyclin A-CDK2, and cyclin D-CDK4 complexes, and **inhibit** kinase activity. X-ray crystallographic data of CDKs, and their complexes with **inhibitors** have played a major role in the success of drug discovery efforts. Combinatorial chemistry, highthroughput screening, functional genomics and informatics have also contributed. CDK **inhibitors** currently under investigation include flavopiridol, olomoucine, roscovitine, puvalanol B, the dihydroindolo[3,2-d][1]benzazepinone kenpaullone, indirubin-3 -monoxime and novel diaminothiazoles such as AG12275. The anticancer therapeutic potential of CDK **inhibitors** has been demonstrated in preclinical studies, and Phases I and II clinical trials in cancer **patients** are currently underway.

```
=> d his

     (FILE 'HOME' ENTERED AT 12:32:25 ON 20 SEP 2004)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:33:13 ON 20 SEP 2004
L1          1263 S AURORA (5W)KINASE?
L2            32 S "AUR-1" OR "AUR-2"
L3          1288 S L1 OR L2
L4           643 S HUMAN AND L3
L5       9998535 S MODULAT? OR INHIBIT? OR ACTIVAT?
L6           298 S L4 AND L5
L7            23 S L6 AND (PATIENT? OR ADMINISTER?)
L8            12 DUP REM L7 (11 DUPLICATES REMOVED)

=> e plowman g/au
E1             2     PLOWMAN F T/AU
E2             1     PLOWMAN F W/AU
E3           107 --> PLOWMAN G/AU
E4           356     PLOWMAN G D/AU
E5             1     PLOWMAN G R/AU
E6             1     PLOWMAN GERGORY D/AU
E7            15     PLOWMAN GREG/AU
E8            10     PLOWMAN GREG D/AU
E9            25     PLOWMAN GREGORY/AU
E10          181     PLOWMAN GREGORY D/AU
E11            1     PLOWMAN GREGORY DEAN/AU
E12            1     PLOWMAN GREGOSY D/AU

=> se3-e10
SE3-E10 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s e3-e10
L9           696 ("PLOWMAN G"/AU OR "PLOWMAN G D"/AU OR "PLOWMAN G R"/AU OR "PLOW
                 MAN GERGORY D"/AU OR "PLOWMAN GREG"/AU OR "PLOWMAN GREG D"/AU
                 OR "PLOWMAN GREGORY"/AU OR "PLOWMAN GREGORY D"/AU)
```

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=> e mossie k/au
E1            1     MOSSICHUK N M/AU
E2            1     MOSSIDIETH V/AU
E3           31 --> MOSSIE K/AU
E4           22     MOSSIE K G/AU
E5           21     MOSSIE KEVIN/AU
E6            9     MOSSIE KEVIN G/AU
E7            1     MOSSIE KEVIN MXOLISI GODWIN/AU
E8            3     MOSSIE R/AU
E9           20     MOSSIE R D/AU
E10           1     MOSSIE RAYMOND D/AU
E11           1     MOSSIEMAN D S/AU
E12           5     MOSSIENKO E V/AU

=> s e3-e7
L10          84 ("MOSSIE K"/AU OR "MOSSIE K G"/AU OR "MOSSIE KEVIN"/AU OR "MOSSI
                E KEVIN G"/AU OR "MOSSIE KEVIN MXOLISI GODWIN"/AU)

=> s l9 or l10
L11         759 L9 OR L10

=> d his

     (FILE 'HOME' ENTERED AT 12:32:25 ON 20 SEP 2004)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:33:13 ON 20 SEP 2004
L1          1263 S AURORA (5W)KINASE?
L2            32 S "AUR-1" OR "AUR-2"
L3          1288 S L1 OR L2
L4           643 S HUMAN AND L3
L5       9998535 S MODULAT? OR INHIBIT? OR ACTIVAT?
L6           298 S L4 AND L5
L7            23 S L6 AND (PATIENT? OR ADMINISTER?)
L8            12 DUP REM L7 (11 DUPLICATES REMOVED)
                 E PLOWMAN G/AU
L9           696 S E3-E10
                 E MOSSIE K/AU
L10           84 S E3-E7
L11          759 S L9 OR L10

=> s l4 and l11
L12          18 L4 AND L11

=> dup rem l12
PROCESSING COMPLETED FOR L12
L13           6 DUP REM L12 (12 DUPLICATES REMOVED)

=> d 1-6 ibib ab

L13  ANSWER 1 OF 6  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2002:488124  HCAPLUS
DOCUMENT NUMBER:          137:59517
TITLE:                    Human AURORA-1 and AURORA
                          -2 kinases, cDNA and amino acid sequences,
                          and recombinant production
INVENTOR(S):              Plowman, Gregory; Mossie, Kevin
PATENT ASSIGNEE(S):       Sugen, Inc., USA
SOURCE:                   U.S. Pat. Appl. Publ., 43 pp., Cont.-in-part of U.S.
                          Ser. No. 5,268, abandoned.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   4
```

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002081578	A1	20020627	US 1998-12135	19980122
US 6716575	B2	20040406		
CN 1205740	A	19990120	CN 1996-199101	19961125
US 5962312	A	19991005	US 1996-755728	19961125
CA 2318352	AA	19990729	CA 1999-2318352	19990121
WO 9937788	A2	19990729	WO 1999-US1283	19990121
WO 9937788	A3	19990930		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9925605	A1	19990809	AU 1999-25605	19990121
EP 1051500	A2	20001115	EP 1999-905450	19990121
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002508937	T2	20020326	JP 2000-528695	19990121
US 6207401	B1	20010327	US 1999-283011	19990331

PRIORITY APPLN. INFO.:	US 1995-8809P	P	19951218
	US 1996-23943P	P	19960814
	US 1996-755728	A2	19961125
	US 1998-5268	B2	19980109
	US 1998-12135	A	19980122
	WO 1999-US1283	W	19990121

AB The invention provides protein and cDNA sequences for **human** AURORA-1 (AUR1) and/or AURORA-2 (AUR2), which are members of serine/threonine kinase family containing short N-terminal extensions. AUR1 mRNA has been shown to be broadly expressed in rapidly dividing cells, derived from both normal and tumor tissues. AUR2 mRNA, however, has been shown to be expressed in a more restricted pattern being low or absent in most normal tissues and abundant in only a subset of tumor-derived cell lines. The invention also demonstrated that AUR1 and AUR2 kinases were able to phosphorylate myelin basic protein. The invention further discussed the possible involvement of AUR1 and AUR2 kinases in cancer and/or other signal transduction disorders, and the possible biol., diagnostic and/or therapeutic uses of these kinases. The AUR1 and AUR2 genes are mapped to chromosome 17p13.1 and 20q13.2 resp. Methods for treatment, diagnosis, and screening are provided for AUR1 and/or AUR2 related diseases or conditions characterized by an abnormal interaction between a AUR1 and/or AUR2 polypeptide and a AUR1 and/or AUR2 binding partner.

L13 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1999:487404 HCAPLUS
DOCUMENT NUMBER:	131:126397
TITLE:	AURORA proteins with sequence similarity to protein tyrosine kinases and cDNAs encoding them and their diagnostic and therapeutic uses
INVENTOR(S):	**Plowman, Gregory D.; Mossie, Kevin**
PATENT ASSIGNEE(S):	Sugen, Inc., USA
SOURCE:	PCT Int. Appl., 153 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9937788	A2	19990729	WO 1999-US1283	19990121
WO 9937788	A3	19990930		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002081578	A1	20020627	US 1998-12135	19980122
US 6716575	B2	20040406		
CA 2318352	AA	19990729	CA 1999-2318352	19990121
AU 9925605	A1	19990809	AU 1999-25605	19990121
EP 1051500	A2	20001115	EP 1999-905450	19990121
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002508937	T2	20020326	JP 2000-528695	19990121
PRIORITY APPLN. INFO.:			US 1998-12135 A	19980122
			US 1995-8809P P	19951218
			US 1996-23943P P	19960814
			US 1996-755728 A2	19961125
			US 1998-5268 B2	19980109
			WO 1999-US1283 W	19990121

AB Two novel proteins, AURORA-1 (**AUR-1**) and AURORA-2 (**AUR-2**) that are members of the protein tyrosine kinase sequence family are identified and cDNAs encoding them are cloned. The proteins may play a role in disease and methods of using them in the diagnosis of disease and in screening for effectors that may be of therapeutic use are described. The cDNAs were cloned by PCR from an array of **human** tissue mRNAs with primers derived from strongly conserved sequences of protein tyrosine kinases. Sequence comparison showed them to be most similar to the Drosophila AURORA gene product. The cDNAs were expressed in COS cells with proteins with mol. wts. consistent with those predicted from the amino acid sequence obtained. The genes were widely expressed in a number of normal tissues and in colorectal cancers. **AUR-2** was mapped to an amplicon of chromosome 20 associated with tumors and overexpression of wild-type and mutant **AUR-2** genes in rat fibroblasts led to an activating mutant causing neoplastic transformation.

L13 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:635436 HCAPLUS
DOCUMENT NUMBER: 131:254328
TITLE: **Human AURORA**-1 and **AURORA**-2 **kinases**, cDNA and amino acid sequences, and recombinant production
INVENTOR(S): **Plowman, Gregory; Mossie, Kevin**
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: U.S., 28 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5962312	A	19991005	US 1996-755728	19961125
US 5972676	A	19991026	US 1997-974655	19971119
US 2002081578	A1	20020627	US 1998-12135	19980122
US 6716575	B2	20040406		

US 6207401	B1	20010327	US 1999-283011		19990331
PRIORITY APPLN. INFO.:			US 1995-8809P	P	19951218
			US 1996-23943P	P	19960814
			US 1996-755728	A3	19961125
			US 1998-5268	B2	19980109
			US 1998-12135	A3	19980122

AB The present invention relates to **human** AURORA-1 (**AUR-1**) and/or AURORA-2 (**AUR-2**) polypeptides, nucleic acids encoding such polypeptides, cells, tissues and animals containing such nucleic acids. The invention also provides a probe for detection of nucleic acids encoding **AUR-1** and/or **AUR-2** polypeptides. The invention further provides an expression vector containing nucleic acids encoding **AUR-1** and/or **AUR-2** polypeptides used for recombinant production of polypeptides in a host cell. The cDNA sequences as well as the corresponding amino acids sequences of **human AUR-1** and **AUR-2** are provided. **AUR-1** and **AUR-2** are related serine/threonine kinases with short N-terminal extensions. AUR1 mRNA has been shown to be broadly expressed in rapidly dividing cells, derived from both normal and tumor tissues. AUR2 mRNA, however, has been shown to be expressed in a more restricted pattern being low or absent in most normal tissues and abundant in only a subset of tumor-derived cell lines. The invention also demonstrated that **AUR-1** and **AUR-2** kinases were able to phosphorylate myelin basic protein. The invention further discussed the possible involvement of **AUR-1** and **AUR-2** kinases in cancer and/or other signal transduction disorders, and the possible biol., diagnostic and/or therapeutic uses of these kinases.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 6 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER:	1999442484 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 10511710
TITLE:	The **Aurora**/Ipl1p **kinase** family: regulators of chromosome segregation and cytokinesis.
AUTHOR:	Bischoff J R; **Plowman G D**
CORPORATE SOURCE:	SUGEN, 230 East Grand Avenue, South San Francisco, CA 94080-4811, USA.. jim-bischoff@sugen.com
SOURCE:	Trends in cell biology, (1999 Nov) 9 (11) 454-9. Ref: 38 Journal code: 9200566. ISSN: 0962-8924.
PUB. COUNTRY:	ENGLAND: United Kingdom
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE) General Review; (REVIEW) (REVIEW, TUTORIAL)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	200001
ENTRY DATE:	Entered STN: 20000114 Last Updated on STN: 20020420 Entered Medline: 20000104

AB Members of the Aurora/Ipl1p family of mitotically regulated serine/threonine kinases are emerging as key regulators of chromosome segregation and cytokinesis. Proper chromosome segregation and cytokinesis ensure that each daughter cell receives the full complement of genetic material. Defects in these processes can lead to aneuploidy and the propagation of genetic abnormalities. This review discusses the **Aurora**/Ipl1p **kinases** in terms of their protein structure and proposed function in mitotic cells and also the potential role of aurora2 in **human** cancer.

L13 ANSWER 5 OF 6 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER:	1998270872 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9606188
TITLE: A homologue of Drosophila **aurora kinase** is oncogenic and amplified in **human** colorectal cancers.
AUTHOR: Bischoff J R; Anderson L; Zhu Y; **Mossie K**; Ng L; Souza B; Schryver B; Flanagan P; Clairvoyant F; Ginther C; Chan C S; Novotny M; Slamon D J; **Plowman G D**
CORPORATE SOURCE: SUGEN, Inc., Redwood City, California 94063, USA.
CONTRACT NUMBER: GM45185 (NIGMS)
SOURCE: EMBO journal, (1998 Jun 1) 17 (11) 3052-65.
Journal code: 8208664. ISSN: 0261-4189.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 19980716
Last Updated on STN: 20020420
Entered Medline: 19980709

AB Genetic and biochemical studies in lower eukaryotes have identified several proteins that ensure accurate segregation of chromosomes. These include the Drosophila **aurora** and yeast Ipl1 **kinases** that are required for centrosome maturation and chromosome segregation. We have identified two **human** homologues of these genes, termed aurora1 and aurora2, that encode cell-cycle-regulated serine/threonine kinases. Here we demonstrate that the aurora2 gene maps to chromosome 20q13, a region amplified in a variety of **human** cancers, including a significant number of colorectal malignancies. We propose that aurora2 may be a target of this amplicon since its DNA is amplified and its RNA overexpressed, in more than 50% of primary colorectal cancers. Furthermore, overexpression of aurora2 transforms rodent fibroblasts. These observations implicate aurora2 as a potential oncogene in many colon, breast and other solid tumors, and identify centrosome-associated proteins as novel targets for cancer therapy.

L13 ANSWER 6 OF 6 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
DUPLICATE 3
ACCESSION NUMBER: 1997-09437 BIOTECHDS
TITLE: Aurora-1 and aurora-2 genes; vector expression in host cell, DNA probe and antibody production by hybridoma cell culture for cancer gene therapy
AUTHOR: **Plowman G D**; **Mossie K G**
PATENT ASSIGNEE: Sugen
LOCATION: Redwood City, CA, USA.
PATENT INFO: WO 9722702 26 Jun 1997
APPLICATION INFO: WO 1996-US18859 25 Nov 1996
PRIORITY INFO: US 1996-23943 14 Aug 1996; US 1995-8809 18 Dec 1995
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1997-341693 [31]

AB An isolated, enriched or purified **human** DNA molecule (I) encoding AURORA-1 (**AUR-1**) and/or **AUR-2** is new. Also claimed are; a DNA probe for the detection of (I) in a sample; a recombinant DNA molecule encoding **AUR-1** and/or **AUR-2** and a vector or promoter effective to initiate transcription in a host cell; a recombinant DNA molecule containing a transcriptional region functional in a cell, a sequence complementary to an RNA sequence encoding **AUR-1** or **AUR-1** and a transcriptional termination region functional in a cell; an isolated, enriched or purified **AUR-1** or **AUR-2**; an antibody having specific binding affinity to **AUR-1** or **AUR-2** ; and a hybridoma cell culture which produces the antibody. The

recombinant molecules can be used to create transgenic animals as an in vivo test system for studying the effects of introducing **AUR-1** and/or **AUR-2** and the effects of regulating the protein. (I) encodes 25-300 residues of the 344 **AUR-1**, or 403 **AUR-2** amino acid protein sequences (specified). The above may be useful for cancer gene therapy. (96pp)

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     (FILE 'HOME' ENTERED AT 12:32:25 ON 20 SEP 2004)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:33:13 ON 20 SEP 2004
L1          1263 S AURORA (5W)KINASE?
L2            32 S "AUR-1" OR "AUR-2"
L3          1288 S L1 OR L2
L4           643 S HUMAN AND L3
L5       9998535 S MODULAT? OR INHIBIT? OR ACTIVAT?
L6           298 S L4 AND L5
L7            23 S L6 AND (PATIENT? OR ADMINISTER?)
L8            12 DUP REM L7 (11 DUPLICATES REMOVED)
                 E PLOWMAN G/AU
L9           696 S E3-E10
                 E MOSSIE K/AU
L10           84 S E3-E7
L11          759 S L9 OR L10
L12           18 S L4 AND L11
L13            6 DUP REM L12 (12 DUPLICATES REMOVED)
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